

WHAT IS CLAIMED:

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1. A method of regulating protein kinase activity comprising:
contacting a protein kinase with biliverdin reductase, or fragments or
variants thereof, under conditions effective to regulate protein kinase activity.
 2. The method according to claim 1, wherein the protein kinase is
a human protein kinase A or human protein kinase C.
 3. The method according to claim 2, wherein the human protein
kinase C is selected from the group of protein kinase C isozymes α , β , and γ .
 4. The method according to claim 2, wherein the biliverdin
reductase is rat or human biliverdin reductase.
 5. The method according to claim 4, wherein the biliverdin
reductase is human biliverdin reductase comprising an amino acid sequence according
to SEQ. ID. No. 1 or SEQ. ID. No. 3.
 6. The method according to claim 4, wherein the biliverdin
reductase is a fragment of rat biliverdin reductase comprising an amino acid sequence
according to SEQ. ID. No. 18 or SEQ. ID. No. 19 or a fragment of human biliverdin
reductase comprising an amino acid sequence according to SEQ. ID. No. 34 or SEQ.
ID. No. 35.
 7. The method according to claim 1, wherein said contacting is
carried out in the cell.
 8. The method according to claim 7, wherein the cell is *in vivo*.
 9. The method according to claim 7, wherein the cell is *in vitro*.

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contacting a cell with biliverdin reductase, or fragments or variants thereof, under conditions effective to regulate cell differentiation, growth, or signaling.

11. The method according to claim 10, wherein said contacting a cell comprises:
delivering the biliverdin reductase, or fragment or variant thereof, into the cell.

12. The method according to claim 11, wherein said delivering the biliverdin reductase, or fragment or variant thereof, into the cell comprises:

providing a liposome comprising the biliverdin reductase, or fragment or variant thereof, and

contacting the cell with the liposome under conditions effective for delivery of the biliverdin reductase, or fragment or variant thereof, into the cell.

13. The method according to claim 11, wherein said delivering the biliverdin reductase, or fragment or variant thereof, into the cell comprises:

- providing a nucleic acid molecule encoding the biliverdin reductase, or fragment or variant thereof, and
- introducing the nucleic acid molecule into the cell under conditions effective to express the biliverdin reductase, or fragment or variant thereof, in the cell.

14. The method according to claim 13, further comprising:
inserting the nucleic acid molecule into an expression vector before
said introducing.

15. The method according to claim 10, wherein the biliverdin reductase is human biliverdin reductase.

16. The method according to claim 15, wherein the human biliverdin reductase has an amino acid sequence of SEQ. ID. No. 1, SEQ. ID. No. 3, or variants thereof.
17. The method according to claim 15, wherein the cell is a human cell.
18. The method according to claim 10, wherein the biliverdin reductase is a fragment of rat biliverdin reductase comprising an amino acid sequence of SEQ. ID. No. 18 or SEQ. ID. No. 19 or a fragment of human biliverdin reductase comprising an amino acid sequence according to SEQ. ID. No. 34 or SEQ. ID. No. 35.
19. The method according to claim 10, wherein the cell is *in vivo*.
20. The method according to claim 10, wherein the cell is *in vitro*.
21. A method of treating cellular dysfunction or disease comprising:
contacting a dysfunctional or diseased cell with biliverdin reductase, or fragment or variant thereof, under conditions effective to treat or immortalize the dysfunctional or diseased cell.
22. The method according to claim 21, wherein said contacting with biliverdin reductase, or fragment or variant thereof, comprises:
delivering the biliverdin reductase, or fragment or variant thereof, into the cell.

providing a liposome comprising the biliverdin reductase, or fragment or variant thereof, and

24. The method according to claim 22, wherein said delivering the biliverdin reductase, or fragment or variant thereof, into the cell comprises:

providing a nucleic acid molecule encoding the biliverdin reductase, or fragment or variant thereof, and

introducing the nucleic acid molecule into the cell under conditions effective to express the biliverdin reductase, or fragment or variant thereof, in the cell.

25. The method according to claim 24, further comprising:
inserting the nucleic acid molecule into an expression vector before
said introducing.

26. The method according to claim 21, wherein the biliverdin reductase is human biliverdin reductase.

27. The method according to claim 26, wherein the human biliverdin reductase comprises an amino acid sequence of SEQ. ID. No. 1 or SEQ. ID. No. 3.

28. The method according to claim 26, wherein the cell is a human cell.

29. The method according to claim 21, wherein the cell is *in vivo*.

30. The method according to claim 29, wherein the dysfunctional or diseased cell is present in a cancerous tumor or lesion and said contacting results in immolating the dysfunctional or diseased cell.

31. The method according to claim 21, wherein the cell is *in vitro*.
32. The method according to claim 21, further comprising:
contacting the dysfunctional or diseased cell with poly(ADP-ribose) polymerase.
33. The method according to claim 32, wherein said contacting with poly(ADP-ribose) polymerase is carried out by delivering the poly(ADP-ribose) polymerase into the cell.
34. The method according to claim 33, wherein said delivering the poly(ADP-ribose) polymerase into the cell comprises:
providing a liposome comprising the poly(ADP-ribose) polymerase
and
contacting the cell with the liposome under conditions effective for delivery of the poly(ADP-ribose) polymerase into the cell.
35. The method according to claim 33, wherein said delivering the poly(ADP-ribose) polymerase into the cell comprises:
providing a nucleic acid molecule encoding the poly(ADP-ribose) polymerase and
introducing the nucleic acid molecule into the cell under conditions effective to express the poly(ADP-ribose) polymerase in the cell.
36. The method according to claim 35, further comprising:
inserting the nucleic acid molecule into an expression vector before said introducing.
37. The method according to claim 21, wherein the dysfunctional or diseased cell is responsible for a disease selected from the group consisting of diabetes mellitus, ischemia, inflammation, central nervous system disorders, cardiovascular disease, Alzheimer's disease, dermatological disease, and cancer

contacting a cell with biliverdin reductase, or fragment or variant thereof, under conditions effective to inhibit cell damage following stroke or an ischemic event.

delivering the biliverdin reductase, or fragment or variant thereof, into the cell.

41. The method according to claim 40, wherein the human biliverdin reductase comprises an amino acid sequence of SEQ. ID. No. 1 or SEQ. ID. No. 3.

43. The method according to claim 38, wherein the cell is *in vivo*.

45. The method according to claim 38, further comprising:
inhibiting the activity of poly (ADP-ribose) polymerase in the cell.

47. A biliverdin reductase fragment or variant comprising:
a biliverdin reductase fragment possessing one or more activities of full length biliverdin reductase; or
a biliverdin reductase variant comprising one or more amino acid substitutions affecting one or more activities of full length biliverdin reductase.

48. The biliverdin reductase fragment or variant according to claim 47, wherein the biliverdin reductase fragment comprises one or more phosphorylation sites, a basic N-terminal domain, a hydrophobic domain, a nucleotide binding domain, an oxidoreductase domain, a substrate binding domain, a leucine zipper, a kinase motif, a nuclear localization signal, a zinc finger domain, a protein kinase C enhancing domain, or protein kinase C inhibiting domain.

49. The biliverdin reductase fragment or variant according to claim 48, wherein the fragment has an amino acid sequence comprising SEQ. ID. No. 18 or SEQ. ID. No. 19.

50. The biliverdin reductase fragment or variant according to claim 47, wherein the biliverdin variant comprises an amino acid substitution in the nucleotide binding domain, the oxidoreductase domain, the substrate binding domain, the nuclear localization signal, or the zinc finger domain.

51. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the nucleotide binding domain is a Gly¹⁷→Ala substitution within the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

53. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the leucine zipper is a Ser¹⁴⁹→Ala substitution within the leucine zipper of the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

54. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the substrate binding domain is a Cys⁷⁴→Ala substitution within a first substrate binding domain or a Lys²⁹⁶→Ala substitution within a second substrate binding domain of the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

55. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the oxidoreductase domain is a Lys⁹²His⁹³→Ala-Ala substitution within the oxidoreductase domain of the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

56. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the nuclear localization signal is a G²²²LKRNR²²⁷→VIGSTG substitution within the nuclear localization signal of the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

57. The biliverdin reductase fragment or variant according to claim 50, wherein the amino acid substitution in the zinc finger domain is a Cys²⁸¹→Ala substitution within the zinc finger domain of the biliverdin reductase protein or polypeptide of SEQ. ID. No. 1 or 3.

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